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WAYS IN WHICH TOXIC SUBSTANCES AFFECT CHOLINERGIC STRUCTURES

[Comment: The paper summarized below was presented by M. Ya. Mikhel'son under the title "The Ways in Which Toxic Substances Affect Cholinergic Structures" at the Fourth Conference on Problems of Industrial Toxicology held 29-30 June 1954 at the Leningrad Institute of Labor Hygiene and Occupational Diseases. This summary was published in Farmakologiya i Toksikologiya, Vol 18, No 2, Moscow, March-April 1955, p 61.]

The inhibition of cholinesterase and the effects exerted on cholinoreceptors are of importance in the mechanism of the action of many poisons. Disturbances of the functioning of cholinergic structures within the cerebral cortex, which are brought about by the action of cholinolytic poisons of the atropine type, can be prevented by substances that have anticholinesterase activity, while on the other hand cholinolytic substances exert a therapeutic effect in poisonings with substances which produce a positive choline action, e.g., organophosphorus insecticides or tetraethyl lead. Cholinomimetic substances (nicotine and arecoline) produce spasms of central origin. Spasms produced by nicotine are removed by nicotinolytic substances of the pentaphen [hydrochloride of the diethylaminoethanol ester of phenylcyclopentanecarboxylic acid] type, while those produced by arecoline are removed by muscarinolytic substances of the atropine type and by diethylaminoacetyl-N-phenothiazine.

Poisons which possess anticholinesterase activity or have an action similar to that of choline produce bronchial spasms, whereas cholinolytic substances remove spasms of this type brought about by poisons. Cholinolytic substances which have a trivalent nitrogen atom exert a pronounced central action on the cerebral cortex and on lower divisions of the central nervous system. Conversion of the nitrogen into the quaternary state by iodomethylation sharply reduces the central action and reinforces the blocking action exerted by drugs of this type at peripheral cholinoreceptors, i.e., at vegetative ganglia, skeletal muscles, and vascular chemoreceptors. The same relationship applies to cholinomimetic substances. Consideration of the mechanisms of action outlined above may be of use in the therapy of effects produced by poisons and the prophylaxis of poisonings with toxic substances encountered in industry.

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